REMARKS

Claims 50-68 are currently pending. Claims 50-68 have been rejected under 35 U.S.C. 101, 112 first paragraph and Claim 51 has been rejected under 35 U.S.C. 112 second paragraph.

Specification

Applicant acknowledges that the Examiner has not considered GeneBank Accession Number O15184, that was listed on the PTO-1449, but not received. Applicants have enclosed a copy of the reference herewith.

The Examiner has identified sequences that apparently appear in the specification without the required SEQ ID NO's. The specification has been amended herein to clarify and/or correct such as follows:

Page 21-23, Table 1I spanning contains sequences that are identified as SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8 (see page 23, lines 15-18); the Table has been amended to clarify SEQ ID NOs.

Pages 24-32, Table 1K contains sequences that are identified as SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33 and SEQ ID NO:34 (see page 24, lines 11-26); the Table has been amended to clarify SEQ ID NOs.

Page 32, lines 41-42 contains amino acid sequences that were inadvertently not identified with SEQ ID NOs. The specification has been amended to correct this and a new Sequence listing is provided herewith.

Pages 33-34, Tables 1L, 1M and 1N are herein corrected to clarify SEQ ID NO identification.

Pages 41-44, Table 2D spanning contains sequences that are identified as SEQ ID NO:10, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 and SEQ ID NO:39 (see page 41, lines 6-14); the Table has been amended to clarify SEQ ID NOs.

Pages 45-46, Table 2E and 2F are herein corrected to clarify SEQ ID NO identification.

Pages 53-55, Table 3F contains sequences that are identified on page 53 lines 6-21; the Table has been amended to clarify SEQ ID NOs.

Page 55, Table 3G is herein corrected to clarify SEQ ID NO identification.

Pages 61-62, Table 4D contains sequences that are identified on page 61, lines 5-14; the Table has been amended to clarify SEQ ID NOs.

Pages 62-63, Tables 4E and 4F are herein corrected to clarify SEQ ID NO identification.

Pages 68-70, Table 5D sequences are identified on page 68, lines 3-14; the Table has been amended to clarify SEQ ID NOs.

Pages 70-74, Tables 5E, 5F, 5G, 5H, 5I, 5J, 5K, 5L, 5M and 5N are herein corrected to clarify SEQ ID NO identification.

Pages 79-80, Table 6D sequences are identified on page 79, lines marked 5-15; the Table has been amended to clarify SEQ ID NOs.

Page 80, Table 6E is herein corrected to clarify SEQ ID NO identification.

Pages 85-86, Table 7D sequences are identified on page 85, lines marked 5-14; the Table has been amended to clarify SEQ ID NOs.

Pages 86-87, Tables 7E and 7F are herein corrected to clarify SEQ ID NO identification.

Pages 101-103, Table 9D sequences are identified on page 100, lines 20-25 to page 101, lines1-6; the Table has been amended to clarify SEQ ID NOs.

Page 103-104, Tables 9E, 9F, 9G and 9H are herein corrected to clarify SEQ ID NO identification.

Page 112-113, Table 10E sequences are identified on page 113 at lines 15-16; the Table has been amended to clarify SEQ ID NOs.

Page 114-115, Table 10G sequences are identified on page 114 at lines 2-14; the Table has been amended to clarify SEQ ID NOs.

Page 116, Table 10H and 10I are herein corrected to clarify SEQ ID NO identification.

Page 201, Tables 12-15 contain sequences that are identified in the far right column of each table as SEQ ID NOs: 108 through 119).

No new matter has been added.

The specification was objected to for containing embedded hyperlinks. The specification is herein amended to delete such hyperlinks, particularly at pages 13, 23-24, 32, 41, 45-46, 52-

53, 55, 61-63, 67-68, 70-74, 78-80, 84-87, 100, 103-104, 113-114 and 116. No new matter has been added.

Claims

Claim 51 has been rejected under 35 U.S.C. 112 second paragraph as being indefinite as the claim pertains to "a mature form" which the Examiner contends is not identified in the application. However, applicants respectfully submit the application states beginning at page 123, line 6: "a "mature" form of a polypeptide or protein include the cleavage of the N-terminal methionine residue encoded by the initiation codon of an ORF, or the proteolytic cleavage of a signal peptide or leader sequence." Further the specification states page 20, line 13: "The most likely cleavage site for a NOV1a peptide is between amino acids 23 and 24, at: VAE-QV." NOV1a and d have the same N-terminal amino acid sequence, see Table 1I, page 21, and therefore the same likely cleavage site, between amino acids 23-24, at VAE-QV. Applicants submit that the recitation is clear in view of the teaching in the specification and requests the rejection be withdrawn.

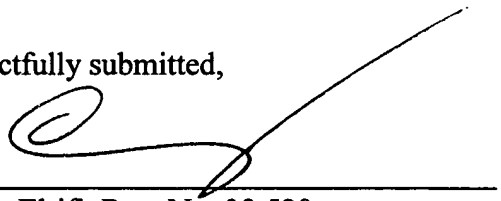
Claims 50-68 have been rejected under 35 U.S.C. 101 as lacking patentable utility. Applicant respectfully disagrees. For example, the application teaches beginning at page 191 methods of detecting quantitative expression of the nucleic acid molecules of the invention in a variety of normal and pathology-derived cells, cell lines and tissues using real time quantitative PCR (RTQ PCR). Results obtaining for the claimed nucleic acids are shown beginning on page 200. Genes that show changes in expression in normal tissues as compared to pathological tissues, for example, are of particular utility. In this regard, Panel 2D results are of particular interest (Table 18, page 206). Table 18 shows the expression of NOV1a and NOV1d as both are recognized by the same probe-primer sets. The panel includes matched sets of malignant and margin kidney tissue from 9 individuals. Strikingly, the normal tissue had consistently higher NOV1 gene expression as compared to the malignant samples. The same pattern is seen in ovarian carcinoma compared to normal tissue. These results are replicated in the attached Appendix A. One of skill in the art would recognize from these results that NOV1 gene expression may be used for example, to differentiate normal from malignant tissues especially for kidney tissues and this provides useful information in working up the diagnosis of a patient thought to have renal cancer. Applicant respectfully requests that the rejection be withdrawn.

Claims 50-68 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. Applicants respectfully disagree. As discussed above, the specification teaches how to determine the expression profile of the claimed nucleic acid molecules and have shown the claimed molecules have an expression pattern particularly useful in differentiating normal from malignant tissues, particularly renal and ovarian tissue. Applicant respectfully requests the rejection be withdrawn.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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Fax: (617) 542 2241

Dated: April 8, 2004

TRA 1905339v1

PANEL 2D

		Ag1313b CT	Relative Expression	Ag708 CT	Relative Ex
1	Normal Colon	30.11	18.40%	31.48	28.30%
2	CC Well to Mod Diff (ODO3866)	31.82	5.60%	34.84	2.80%
3	CC Margin (ODO3866)	32.42	3.70%	37.31	0.50%
4	CC Gr.2 rectosigmoid (ODO3868)	33.05	2.40%	38.4	0.20%
5	CC Margin (ODO3868)	36.47	0.20%	37.24	0.50%
6	CC Mod Diff (ODO3920)	36.9	0.20%	40	0%
7	CC Margin (ODO3920)	34.14	1.10%	36.68	0.80%
8	CC Gr.2 ascend colon (ODO3921)	32.39	3.80%	35.63	1.60%
9	CC Margin (ODO3921)	33.53	1.70%	35.32	2%
10	CC from Partial Hepatectomy (ODO4309) Mets	34.45	0.90%	36.75	0.70%
11	Liver Margin (ODO4309)	36.62	0.20%	40	0%
12	Colon mets to lung (OD04451-01)	33.28	2%	36.13	1.10%
13	Lung Margin (OD04451-02)	40	0%	40	0%
14	Normal Prostate 6546-1	33.61	1.60%	40	0%
15	Prostate Cancer (OD04410)	36.1	0.30%	38.54	0.20%
16	Prostate Margin (OD04410)	40	0%	40	0%
17	Prostate Cancer (OD04720-01)	38.59	0.10%	38.33	0.20%
18	Prostate Margin (OD04720-02)	34.2	1.10%	37.04	0.60%
19	Normal Lung	32.08	4.70%	34.59	3.30%
20	Lung Met to Muscle (ODO4286)	30.49	14.20%	32.58	13.20%
21	Muscle Margin (ODO4286)	35.74	0.40%	36.03	1.20%
22	Lung Malignant Cancer (OD03126)	32.41	3.70%	33.27	8.20%
23	Lung Margin (OD03126)	34.63	0.80%	36.73	0.70%
24	Lung Cancer (OD04404)	31.87	5.40%	32.75	11.70%
25	Lung Margin (OD04404)	32.36	3.90%	34.27	4.10%
26	Lung Cancer (OD04565)	31.15	9%	34.03	4.80%
27	Lung Margin (OD04565)	40	0%	40	0%
28	Lung Cancer (OD04237-01)	31.43	7.40%	34.59	3.30%
29	Lung Margin (OD04237-02)	35.21	0.50%	35.78	1.40%
30	Ocular Mel Met to Liver (ODO4310)	40	0%	40	0%
31	Liver Margin (ODO4310)	40	0%	40	0%
32	Melanoma Metastasis	28.88	43.20%	30.71	48.30%
33	Lung Margin (OD04321)	37.06	0.10%	38.37	0.20%
34	Normal Kidney	27.67	100%	29.66	100%
35	Kidney Ca, Nuclear grade 2 (OD04338)	30.09	18.70%	33.04	9.60%
36	Kidney Margin (OD04338)	29.49	28.30%	31.4	29.90%
37	Kidney Ca Nuclear grade 1/2 (OD04339)	30.94	10.40%	32.72	12%
38	Kidney Margin (OD04339)	29.23	33.90%	31.41	29.70%
39	Kidney Ca, Clear cell type (OD04340)	32.54	3.40%	34.72	3%
40	Kidney Margin (OD04340)	29.19	34.90%	31.05	38.20%
41	Kidney Ca, Nuclear grade 3 (OD04348)	30.24	16.80%	32.27	16.40%
42	Kidney Margin (OD04348)	29.16	35.60%	31.18	34.90%
43	Kidney Cancer (OD04622-01)	35.63	0.40%	40	0%
44	Kidney Margin (OD04622-03)	32.09	4.70%	33.98	5%
45	Kidney Cancer (OD04450-01)	29.88	21.60%	32.31	15.90%
46	Kidney Margin (OD04450-03)	29.04	38.70%	31.06	37.90%
47	Kidney Cancer 8120607	36.08	0.30%	40	0%
48	Kidney Margin 8120608	31.32	8%	33.33	7.90%
49	Kidney Cancer 8120613	33.11	2.30%	35.19	2.20%

50	Kidney Margin 8120614	30.37	15.40%	31.78	23%
51	Kidney Cancer 9010320	30.83	11.20%	32.57	13.30%
52	Kidney Margin 9010321	29.37	30.80%	31.38	30.40%
53	Normal Uterus	31.45	7.30%	32.75	11.70%
54	Uterine Cancer 064011	32.22	4.30%	34.31	4%
55	Normal Thyroid	35.09	0.60%	37.76	0.40%
56	Thyroid Cancer	40	0%	40	0%
57	Thyroid Cancer A302152	33.99	1.30%	38.19	0.30%
58	Thyroid Margin A302153	33.35	2%	35.19	2.20%
59	Normal Breast	32.57	3.30%	35.32	2%
60	Breast Cancer	32.57	3.30%	34.68	3.10%
61	Breast Cancer (OD04590-01)	32.09	4.70%	33.37	7.60%
62	Breast Cancer Mets (OD04590-03)	31.67	6.30%	34.21	4.30%
63	Breast Cancer Metastasis	34.72	0.80%	37.78	0.40%
64	Breast Cancer	32.26	4.20%	33.87	5.40%
65	Breast Cancer	31.96	5.10%	33.85	5.50%
66	Breast Cancer 9100266	32.59	3.30%	34.31	4%
67	Breast Margin 9100265	32.5	3.50%	34.41	3.70%
68	Breast Cancer A209073	31.7	6.10%	34.06	4.70%
69	Breast Margin A209073	32.01	4.90%	34.27	4.10%
70	Normal Liver	40	0%	40	0%
71	Liver Cancer	38	0.10%	40	0%
72	Liver Cancer 1025	40	0%	40	0%
73	Liver Cancer 1026	33.29	2%	34.98	2.50%
74	Liver Cancer 6004-T	40	0%	40	0%
75	Liver Tissue 6004-N	35.8	0.40%	40	0%
76	Liver Cancer 6005-T	33.32	2%	34.64	3.20%
77	Liver Tissue 6005-N	40	0%	40	0%
78	Normal Bladder	31.68	6.20%	33.63	6.40%
79	Bladder Cancer	33.19	2.20%	36.02	1.20%
80	Bladder Cancer	31.52	6.90%	33.7	6.10%
81	Bladder Cancer (OD04718-01)	30.42	14.90%	32.54	13.60%
82	Bladder Normal Adjacent (OD04718-03)	31.04	9.70%	33.19	8.70%
83	Normal Ovary	28.4	60.30%	30.03	77.40%
84	Ovarian Cancer	29.3	32.30%	31.27	32.80%
85	Ovarian Cancer (OD04768-07)	34.58	0.80%	36.68	0.80%
86	Ovary Margin (OD04768-08)	30.96	10.20%	32.72	12%
87	Normal Stomach	33.08	2.40%	34.76	2.90%
88	Gastric Cancer 9060358	34.16	1.10%	36.13	1.10%
89	Stomach Margin 9060359	32.48	3.60%	33.74	5.90%
90	Gastric Cancer 9060395	36.31	0.30%	37.55	0.40%
91	Stomach Margin 9060394	34.14	1.10%	35.45	1.80%
92	Gastric Cancer 9060397	31.81	5.70%	33.08	9.30%
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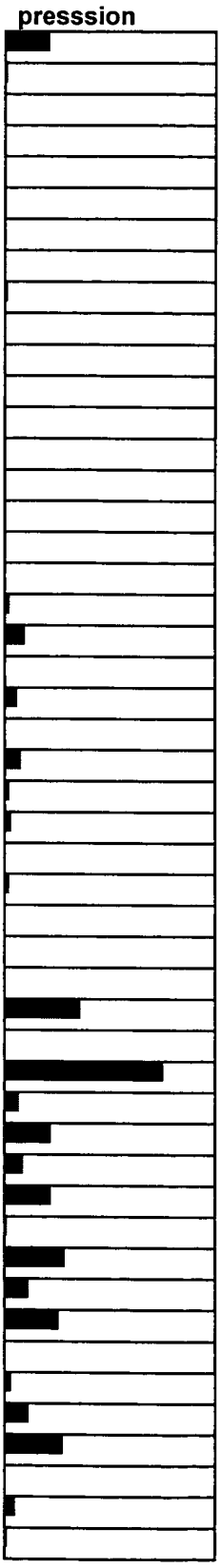
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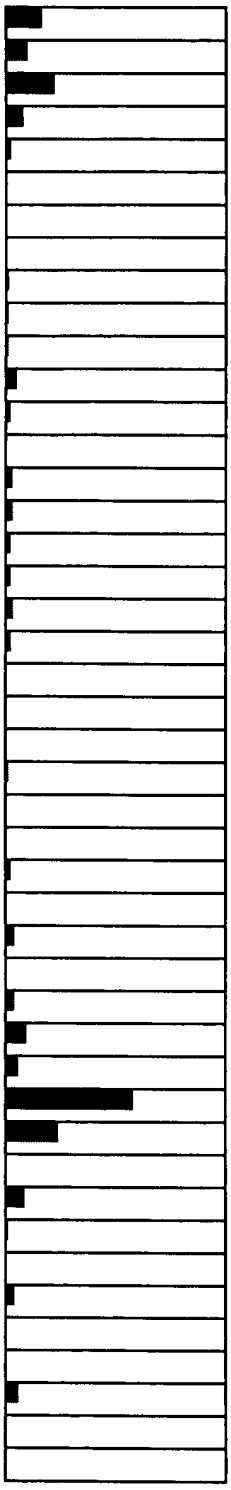

C62

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  TITLE     Generation and initial analysis of more than 15,000 full-length
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  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)
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AUTHORS Lee,J.W., Choi,H.S., Gyuris,J., Brent,R. and Moore,D.D.
TITLE Two classes of proteins dependent on either the presence or absence of thyroid hormone for interaction with the thyroid hormone receptor
JOURNAL Mol. Endocrinol. 9 (2), 243-254 (1995)
MEDLINE 95295737
PUBMED 7776974
REMARK SEQUENCE OF 431-545 FROM N.A.
COMMENT On Apr 1, 2002 this sequence version replaced gi:2499059.

[FUNCTION] May act as a link between CDC42 signaling and regulation of the actin cytoskeleton.
[SUBUNIT] Specifically interact with the ligand binding domain of the thyroid receptor (TR). Requires the presence of thyroid hormone for its interaction. Binds to CDC42.
[TISSUE SPECIFICITY] Expressed most abundantly in skeletal muscle, heart and placenta, present at lower levels in pancreas, lung, liver, and kidney, and barely detectable in brain.
[SIMILARITY] Contains 1 FCH domain.
[SIMILARITY] Contains 1 SH3 domain.

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